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Hypocalcaemia as a Consequence of Blood Transfusion in the Patients with Liver Impairment and General Approaches for the Management

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ABSTRACT

Background: Hypocalcaemia is a potentially life-threatening complication of blood transfusion, especially in patients with liver dysfunction. Citrate in stored blood products chelates ionized calcium (Ca^{2+}). In liver-impaired patients, reduced citrate metabolism leads to citrate accumulation and prolonged hypocalcaemia, which may impair cardiac, neuromuscular, and coagulation functions. **Methodology:** A retrospective observational study was conducted on 150 adult patients with liver impairment who underwent blood transfusion (whole blood, PRBCs, FFP, and platelets). Serum calcium levels were measured at baseline and up to 48 hours post-transfusion. Patient demographics, transfusion details, onset of hypocalcaemia, clinical manifestations, and calcium supplementation were recorded. Statistical analysis was performed to determine correlations and predictors of hypocalcaemia. **Results:** Among 150 patients, 52.6% developed moderate hypocalcaemia, 32% mild, and 15.3% severe hypocalcaemia. The onset most occurred commonly 6–24 hours after transfusion. A significant inverse correlation was observed between transfusion units and serum calcium levels ($r = -0.496$, $p < 0.001$). Whole blood and PRBCs were most associated with calcium depletion. Symptoms ranged from muscle cramps to arrhythmias. Intravenous calcium chloride was commonly used, with 37.3% of patients achieving normocalcaemia within 24–48 hours. **Conclusion:** Transfusion-associated hypocalcaemia is common and clinically significant in patients with liver impairment, especially with multiple citrate-rich transfusions. Reduced hepatic citrate metabolism increases the risk of prolonged calcium chelation and related complications. Routine ionized calcium monitoring and early intravenous calcium supplementation are essential to improve patient outcomes.

Keywords: Hypocalcaemia, Blood transfusion, Liver impairment, Citrate toxicity, Ionized calcium

INTRODUCTION

Back ground of Hypocalcaemia

Normal calcium physiology and its role in the body

Calcium plays a vital role in skeletal mineralization, with over 99% stored in bones as hydroxyapatite. In serum, calcium exists in three forms: protein-bound (40%), complexed (9%), and ionized (51%). Ionized calcium is the biologically active form responsible for maintaining normal physiological functions [1]. Parathyroid hormone (PTH), vitamin D, and calcitonin regulate the absorption, distribution, and excretion of Calcium ions especially within the intestines and kidneys [2].

Definition and overview of Hypocalcaemia

Hypocalcaemia is defined as a reduction in serum ionized calcium levels (<2.12mmol/L), with normal total serum calcium around 8.5 mg/dL [3,4]. It is a potentially life-threatening condition that may result from disruptions in calcium homeostasis, including deficiency or resistance to parathyroid hormone (PTH), vitamin D deficiency, or abnormalities in the calcium-sensing receptor (CaSR) [5,6]. Severe hypocalcaemia can cause neuromuscular irritability, tetany, seizures, and cardiac complications, and is typically treated with intravenous calcium gluconate [7]. While some patients remain asymptomatic, others may develop symptoms ranging from muscle cramps and dry skin to paresthesia, muscle spasms, arrhythmias, and heart failure in severe cases [8].

Epidemiology of Hypocalcaemia Due to Blood Transfusion in Liver-Impaired Patients:

Hypocalcaemia is a common complication during and after blood transfusion, particularly in patients with liver dysfunction. The incidence in critically ill or liver-impaired patients ranges from 30–70%, depending on transfusion volume, type of blood product, and severity of liver disease [9]. In developed countries, studies report ionized hypocalcaemia in 30–60% of liver-impaired patients undergoing transfusion [10]. In low- and middle-income countries, limited monitoring may lead to under recognition, with a Southeast Asian study reporting hypocalcaemia in 68% of transfused cirrhotic patients [11]. The incidence is even higher in trauma and ICU settings using massive transfusion protocols, where nearly 70% of liver-impaired patients develop moderate to severe hypocalcaemia.

Mechanism of Hypocalcaemia in Blood transfusion - Citrate anticoagulation and its role in calcium chelation

Stored blood products contain citrate as an anticoagulant, which chelates ionized calcium (Ca^{2+}) and prevents coagulation [9]. In healthy individuals, the liver rapidly metabolizes citrate; however, rapid transfusion or liver dysfunction can lead to citrate accumulation and reduced plasma ionized calcium levels [12]. During large or rapid transfusions, circulating citrate continues to bind calcium, decreasing its availability and resulting in transfusion-induced hypocalcaemia [13,14].

METHODOLOGY

Study Design

A retrospective observational study conducted in patients with liver impairment who underwent blood transfusion to assess changes in serum calcium levels.

Study Area

Conducted at Narayana Medical College and Hospital, a 1200-bedded multidisciplinary hospital in Chintareddypalem, Nellore, Andhra Pradesh.

Study Duration

6 months (October 2024 – April 2025).

Sample Size

Approximately 100–150 patient records were reviewed. These included liver-impaired patients who received blood transfusions, selected based on availability of complete data to evaluate post-transfusion hypocalcaemia.

Inclusion Criteria

1. Confirmed liver impairment (e.g., cirrhosis, hepatitis, NAFLD)
2. History of blood transfusion
3. Normal pre-transfusion calcium with documented post-transfusion levels
4. Age ≥18 years (or as per study)

Exclusion Criteria

1. Pre-existing hypocalcaemia
2. Parathyroid disorders
3. Severe vitamin D deficiency
4. Renal impairment (AKI/ESRD)
5. Use of calcium-altering medications

Sample Estimation

Data were collected from inpatient records of liver-impaired patients who received transfusions over a 6-month period to assess serum calcium abnormalities.

1) Informed Consent (Annexure I):

Patient details and laboratory data were collected after obtaining informed consent.

2) Patient Data Collection Form (Annexure II):

A structured form was used to record patient demographics, clinical details, and laboratory parameters.

3) Liver Impairment Grading Scale (Annexure III): Child-Pugh or MELD score was used to assess liver disease severity and correlate it with the risk of hypocalcaemia.

4) Questionnaire Form (Annexure IV):

A structured questionnaire was used to record symptoms, clinical signs, transfusion details, and treatment related to hypocalcaemia.

Sampling Method and Recruitment Process:

Data were extracted from patient records using defined inclusion and exclusion criteria and convenience sampling. Eligible liver-impaired patients who received blood transfusions were identified through the Medical Records Department. Case files were reviewed to verify eligibility and collect data. Ethical clearance was obtained prior to the study.

Study Procedure:

The study was initiated after Institutional Ethics Committee approval. Eligible patients were retrospectively selected, and data were collected with informed consent. Information on demographics, transfusion details, liver function grading, and pre- and post-transfusion calcium levels was recorded to assess hypocalcaemia.

Data Collection:

Data included serum ionized calcium, LFTs, transfusion details (type, volume, units), hypocalcaemia symptoms, medications, and comorbidities. Measurements were recorded at baseline, and 6, 12, and 24hours post-transfusion.

Data Management:

Data were anonymized, securely stored, and systematically organized. Records were verified for completeness and accuracy to ensure reliability.

Data Analysis:

Descriptive and inferential statistics were applied to evaluate calcium trends and their association with liver function and transfusion parameters, identifying prevalence and risk factors.

Ethical Considerations:

Ethical approval was obtained from the Institutional Ethics Committee prior to the study. Informed consent was taken from all participants or legal guardians after explaining the study purpose. Patient confidentiality was strictly maintained through anonymization and secure data handling. The study adhered to institutional guidelines and the Declaration of Helsinki, ensuring protection of patient rights, safety, and data privacy.

RESULTS

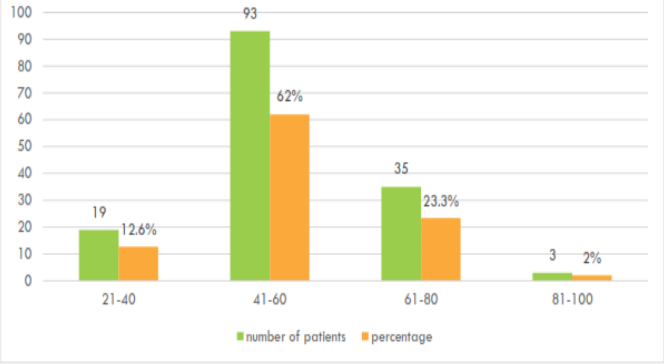

Fig.1: Graphical representation based on Age groups

Table.1: Patients distribution based on different age groups

AGE	NUMBER OF PATIENTS	PERCENTAGE (%)
21-40	19	12.6%
41-60	93	62%
61-80	35	23.3%
81-100	3	2%

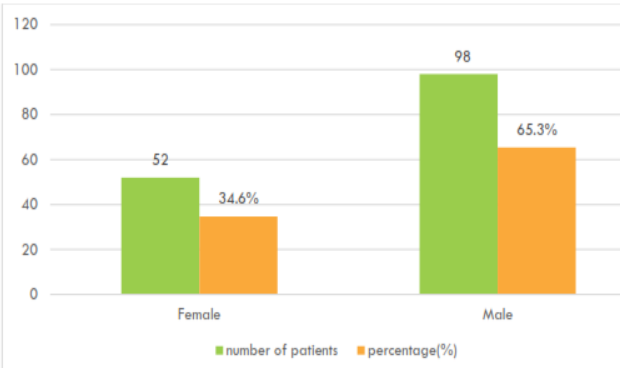

Fig.2: Graphical representation based on Gender

Table 2: Patients distribution based on gender

GENDER	NUMBER OF PATIENTS	PERCENTAGE (%)
Male	98	65.3%
Female	52	34.6%

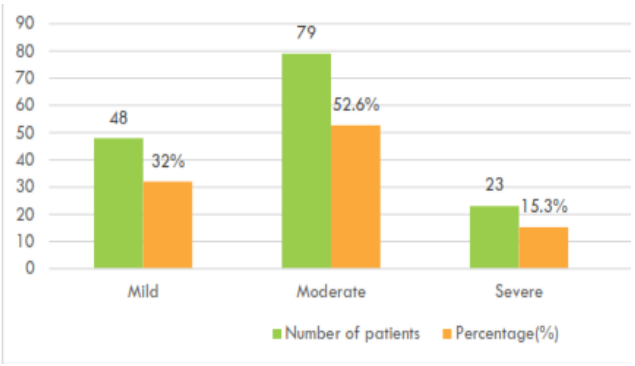

Fig.3: Graphical representation based on the severity of Hypocalcemia

Table 3: Patients distribution based on Hypocalcemia Severity

CATEGORY	NUMBER OF PATIENTS	PERCENTAGE (%)
Mild	48	32%
Moderate	79	52.6%
Severe	23	15.3%

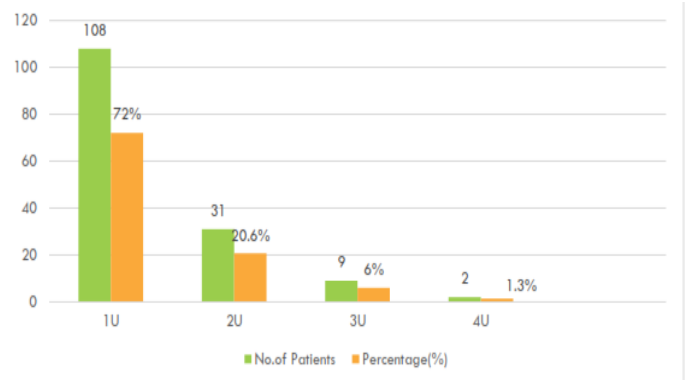

Fig.4: Graphical representation of the patients based on the units of blood transfused

Table 4: Patients distributed based on the units of blood transfused

NUMBER OF UNITS OF BLOOD TRANSFUSED	NUMBER OF PATIENTS	PERCENTAGE (%)
1U	108	72
2U	31	20.6
3U	9	6
4U	2	1.3

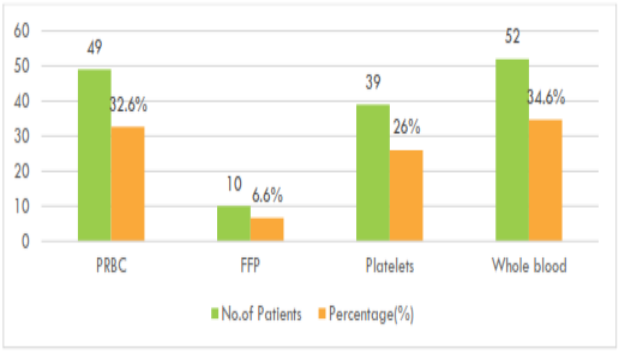

Fig.5: Graphical representation of the patients based on the type of Blood transfused

Fig.6: Patient's distribution based on the type of blood component

BLOOD COMPONENT	NUMBER OF PATIENTS	PERCENTAGE (%)
PRBC	49	32.6%
FFP	10	6.6%
Platelets	39	26%
Whole blood	52	34.6%

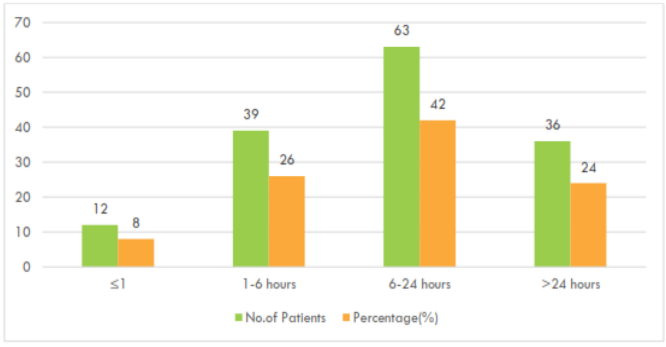

Fig.6: Graphical representation of the patients based on the onset of Hypocalcaemia Post transfusion

Table 6: Patients distribution based on the onset of Hypocalcaemia Post transfusion

TIME PERIOD	NUMBER OF PATIENTS	PERCENTAGE (%)
≤1	12	8%
1-6 hours	39	26%
6-24 hours	63	42%

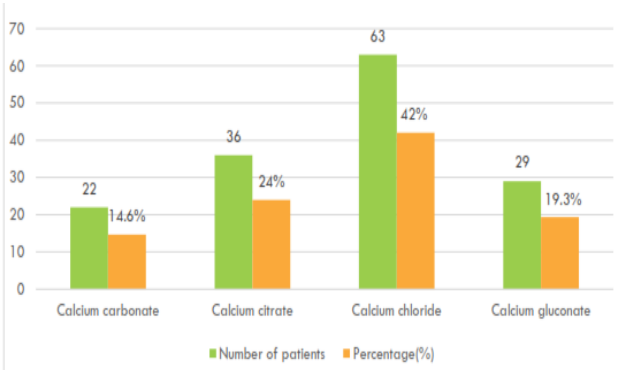

Fig. 7: Graphical representation of the patients based on the drug given

Table 7: Patients distribution based on the drug given

NAME OF THE DRUG	NUMBER OF PATIENTS	PERCENTAGE (%)
Calcium carbonate	22	14.6%
Calcium citrate	36	24%
Calcium chloride	63	42%
Calcium gluconate	29	19.3%

DISCUSSION

This study evaluated the prevalence, severity, and risk factors of hypocalcaemia in liver-impaired patients receiving blood

transfusions. Most patients were aged 41–60 years (62%) with male predominance (65.3%). Moderate hypocalcaemia was most common (52.6%), followed by mild (32%) and severe (15.3%). The majority of the cases occurred 6–24 hours post-transfusion (42%), indicating a delayed onset. A significant moderate negative correlation was observed between transfusion volume and calcium levels ($r = -0.496$, $p < 0.001$), showing that higher transfusion volumes increase the risk of hypocalcaemia due to citrate overload. Whole blood (34.6%) and PRBCs (32.6%) were the most frequently used components, contributing to hypocalcaemia due to high citrate content. Calcium chloride (42%) was the most commonly used treatment, with IV administration preferred (61.3%). Most patients normalized calcium levels within 24–48 hours (37.3%), though some showed delayed recovery (28.6%). Liver cirrhosis and alcoholic cirrhosis (40.6%) were the most common conditions, highlighting impaired citrate metabolism as a major contributing factor, along with the increasing role of fatty liver disease (16.6%).

CONCLUSION

Transfusion-associated hypocalcaemia is a significant risk in liver-impaired patients, especially with multiple units of whole blood or PRBCs. A clear association exists between transfusion volume and severity of calcium reduction, highlighting the need for routine monitoring and early correction. Prompt intravenous calcium supplementation can help prevent complications. Further multicentric, controlled studies with comprehensive biochemical analysis are needed to validate findings and establish standardized transfusion protocols.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

FUNDING

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AI TOOL DECLARATION

The authors declare that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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